

In the Specification

Please substitute the following paragraph on page 11, beginning at line 29:

Fig. 1 schematically depicts the structure of clusterin (based on Rosenberg and Silkensen, 1995). (A) is the precursor polypeptide, (B) is a representation of the mature polypeptide, which is a heterodimeric glycoprotein of 75-80 kDa formed by an α (34-36 kDa) and β (36-39 kDa) chain linked in antiparallel by 5 disulfide bridges near their centers, (C) shows the sequence of human clusterin precursor (SEQ ID NO:1).

Please substitute the following paragraphs on page 8, beginning at line 21:

Heparin, refers to a highly acidic mucopolysaccharide formed of equal parts of sulfated D-glucosamine and D-glucuronic acid with sulfaminic bridges. The molecular weight ranges from six to twenty thousand. Heparin occurs in and is obtained from liver, lung, mast cells, etc., of vertebrates. Its function is unknown, but it is used to prevent blood clotting in vivo and vitro, in the form of many different salts (Medical Subject Headings (MESH), <http://www.nlm.nih.gov/mesh/meshhome.html> see Worldwide Website: <http://www.nlm.nih.gov/mesh/meshhome.html>). Heparin sodium (trade names: Lipo-Hepin and Liquaemin) is used as an anticoagulant in the treatment of thrombosis.

Low molecular weight heparins (LMWHs), heparin fractions, also exist. They have a molecular weight usually between 4000 and 6000 kD. These low-molecular-weight fractions are effective antithrombotic agents. Their administration reduces the risk of hemorrhage, they have a longer half-life, and their platelet interactions are reduced in comparison to unfractionated heparin. They also provide an effective prophylaxis against postoperative major pulmonary embolism (Medical Subject Headings (MESH), <http://www.nlm.nih.gov/mesh/meshhome.html> see Worldwide Website: <http://www.nlm.nih.gov/mesh/meshhome.html>). LMWHs can be e.g nadroparin, N-acetylheparin, ardeparin, certoparin, dalteparin, enoxaparin, reviparin, tinzaparin.

Please substitute the following paragraph on page 11, beginning at line 7:

The ~~treatment~~ treatment of PNS diseases with clusterin has not yet been considered in the art.

Please substitute the following paragraph on page 20, beginning at line 3:

Methods for comparing the identity and homology of two or more sequences are well known in the art. Thus for instance, programs available in the Wisconsin Sequence Analysis Package, version 9.1 (Devereux et al., 1984), for example the programs BESTFIT and GAP, may be used to determine the % identity between two polynucleotides and the % identity and the % homology between two polypeptide sequences. BESTFIT uses the "local homology" algorithm of Smith and Waterman (Smith and Waterman, 1981) and finds the best single region of similarity between two sequences. Other programs for determining identity and/or similarity between sequences are also known in the art, for instance the BLAST family of programs (Altschul et al., 1990; Altschul et al., 1997), accessible through the home page of the NCBI at ~~www.ncbi.nlm.nih.gov~~ Worldwide Website: ncbi.nlm.nih.gov and FASTA (Pearson, 1990; Pearson and Lipman, 1988).

Please substitute the following paragraph on page 24, beginning at line 6:

In a further preferred embodiment of the invention, the fused protein comprises an immunoglobulin (Ig) fusion. The fusion may be direct, or via a short linker peptide which can be as short as 1 to 3 amino acid residues in length or longer, for example, 13 amino acid residues in length. Said linker may be a tripeptide of the sequence E-F-M (Glu-Phe-Met), for example, or a 13-amino acid linker sequence comprising Glu-Phe-Gly-Ala-Gly-Leu-Val-Leu-Gly-Gly-Gln-Phe-Met (SEQ ID NO:2) introduced between clusterin sequence and the immunoglobulin sequence, for instance. The resulting fusion protein has improved properties, such as an extended residence time in body fluids (half-life), or an increased specific activity, increased expression level. The Ig fusion may also facilitate purification of the fused protein.

Please substitute the following paragraph on page 27, beginning at line 15:

The invention further relates to pharmaceutical compositions, particularly useful for prevention and/or treatment of peripheral neurological diseases, which comprise a therapeutically effective amount of clusterin and a therapeutically effective amount of ~~an Heparin~~ a Heparin, optionally further a therapeutically effective amount of an immuno-suppressant.

Please substitute the following paragraph on page 37, beginning at line 17:

After the four weeks of treatment, described in example 3, mice were anesthetized and sacrificed. The contralateral and ipsilateral gastrocnemius muscles were collected and analyzed for choline acetyl transferase (ChAT) activity, ~~a indicator~~ an indicator of neuronal innervation. The ChAT activity was measured accordingly to the protocol described by Contreras et al. (Contreras et al., 1995) except that cold acetyl-CoA was omitted and 0.25nmol of ³H-acetyl-CoA corresponding to 0.05 µCi were added.

Please replace pages 1-3 (Sequence Listing) with new pages 1-3 attached hereto.